Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (currently amended) A composition comprising:
   (a) a virus-like particle; and
   (b) at least one immunostimulatory substance;
   wherein said immunostimulatory substance is ~~bound to~~ packaged into said virus-like particle, and wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide, wherein the CpG motif of said unmethylated CpG-containing oligonucleotide is part of a palindromic sequence, and wherein said palindromic sequence is flanked at its 3'-terminus and at its 5'-terminus by less than 10 guanosine entities.

2. (original) The composition of claim 1 further comprising at least one antigen or antigenic determinant, wherein said antigen or antigenic determinant is bound to said virus-like particle.

3. (currently amended) The composition of claim 2, wherein said ~~at least one~~ antigen or antigenic determinant is bound to said virus-like particle by at least one nonpeptide covalent bond~~, preferably wherein said covalent bond is a non-peptide bond~~.

4. (cancelled)

5. (currently amended) The composition of ~~any one of~~ claims 2 ~~to 4~~, wherein said virus-like particle comprises at least one first attachment site and wherein said antigen or antigenic determinant further comprises at least one second attachment site being selected from the group consisting of:

(a) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(b) an attachment site naturally occurring with said antigen or antigenic determinant;

and wherein said binding of said antigen or antigenic determinant to said virus-like particle is effected through association between said first attachment site and said second attachment site, wherein ~~preferably~~ said association is through at least one non-peptide bond, and wherein said antigen or antigenic determinant and said virus-like particle interact through said association to form an ordered and repetitive antigen array.

6. (cancelled)

7. (currently amended) The composition of claim 5 ~~or 6~~, wherein said first attachment site comprises~~, or preferably consists of,~~ an amino group or a lysine residue.

8. (currently amended) The composition of ~~any of the~~ claims 5 ~~to 7~~, wherein said second attachment site comprises~~, or preferably consists of,~~ a sulfhydryl group or a cysteine residue.

9. (cancelled)

10. (currently amended) The composition of ~~any of the~~ claims 5 ~~to 9~~, wherein said first attachment site is an amino group and said second attachment site is a sulfhydryl group.

11. (currently amended) The composition of ~~any one of~~ claims 2 ~~to 10~~, wherein said antigen is selected from the group consisting of:

(a) polypeptides;

(b) carbohydrates;

(c) steroid hormones; and

(d) organic molecules.

12. (cancelled)

13. (currently amended) The composition of ~~any one of~~ claims 2 ~~to 1~~, wherein said antigen is derived from the group consisting of:

(a) viruses;

(b) bacteria;

(c) parasites;

(d) prions;

(e) tumors;

(f) self-molecules;

(g) non-peptidic hapten molecules

(h) allergens; and

(i) hormones.

14. (currently amended) The composition of claim 13, wherein said antigen is a tumor antigen, ~~and~~ wherein ~~preferably~~ said tumor antigen is selected from the group consisting of:

(a) Her2;

(b) GD2;

(c) EGF-R;

(d) CEA;

(e) CD52;

(f) CD21;

(g) human melanoma protein gp100;

(h) human melanoma protein melan-A/MART-1;

(i) tyrosinase;

(j) NA17-A nt protein;

(k) MAGE-3 protein;

(l) p53 protein;

(m) HPV16 E7 protein;

(n) human melanoma MelanA peptide;

(o) human melanoma MelanA peptide analogue;

(p) HIV polypeptide; and

(q) antigenic fragments of any of the tumor antigens from (a) to (p).

15. (currently amended) The composition of ~~any one of~~ claims 2 ~~to 14~~, wherein said antigen is bound to said virus-like particle by way of a linking sequence.

16. (currently amended) The composition of ~~any one of~~ claims 2 ~~to 15~~, wherein said antigen comprises a cytotoxic T cell epitope, a Th cell epitope or a combination of at least two of said epitopes, wherein said at least two epitopes are bound directly or by way of a linking sequence, and wherein ~~preferably~~ said cytotoxic T cell epitope is a viral or a tumor cytotoxic T cell epitope.

17. (currently amended) The composition of ~~any one of the preceding~~ claims 1, wherein said unmethylated CpG-containing oligonucleotide comprises 10 to 30 nucleotides.

18. (currently amended) The composition of ~~any one of the preceding~~ claims 1, wherein said palindromic sequence is GACGATCGTC (SEQ ID NO: 1).

19. (currently amended) The composition of ~~any one of the preceding~~ claims 1, wherein said palindromic sequence is flanked at its 5'-terminus by at least 3 and at most 9 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus by at least 6 and at most 9 guanosine entities.

20. (currently amended) The composition of claim 18, wherein said unmethylated CpG-containing oligonucleotide has a nucleic acid sequence selected from

(a) GGGGACGATCGTCGGGGGG ((SEQ ID NO: 2);

(b) GGGGGACGATCGTCGGGGGG ((SEQ ID NO: 3);

(c) GGGGGGACGATCGTCGGGGGG ((SEQ ID NO: 4);

(d) GGGGGGGACGATCGTCGGGGGG ((SEQ ID NO: 5);

(e) GGGGGGGGACGATCGTCGGGGGGG ((SEQ ID NO:6);

(f) GGGGGGGGGACGATCGTCGGGGGGGG ((SEQ ID NO: 7);

(g) GGGGGGGGGGACGATCGTCGGGGGGGGG ((SEQ ID NO: 8); and

(h) GGGGGGCGACGACGATCGTCGTCGGGGGGG ((SEQ ID NO: 9).

21. (cancelled).

22. (cancelled)

23. (cancelled)

24. (cancelled)

25. (cancelled)

26. (cancelled)

27. (cancelled)

28. (cancelled)

29. (cancelled)

30. (cancelled)

31. (cancelled)

32. (currently amended) The composition of ~~any one of the preceding~~ claims 1, wherein said virus-like particle is selected from the group consisting of:

(a) recombinant proteins of Hepatitis B virus;
(b) recombinant proteins of measles virus;
(c) recombinant proteins of Sinbis virus;
(d) recombinant proteins of Rotavirus;
(e) recombinant proteins of Foot-and-Mouth-Disease virus;
(f) recombinant proteins of Retrovirus;
(g) recombinant proteins of Norwalk virus;
(h) recombinant proteins of human Papilloma virus;
(i) recombinant proteins of BK virus;
(j) recombinant proteins of bacteriophages;
(k) recombinant proteins of RNA-phages;
(l) recombinant proteins of Qβ-phage;
(m) recombinant proteins of GA-phage;
(n) recombinant proteins of fr-phage;
(o) recombinant proteins of AP 205-phage;
(p) recombinant proteins of Ty; and
(q) fragments of any of the recombinant proteins from (a) to (p).

33. (cancelled)

34. (currently amended) The composition of ~~any one of~~ claims 1 ~~to 32~~, wherein said virus-like particle comprises~~, or alternatively consists essentially of, or alternatively consists of~~ recombinant proteins, or fragments thereof, of a RNA-

phage, wherein ~~preferably~~ said RNA-phage is selected from the group consisting of:

(a) bacteriophage Qβ;
(b) bacteriophage R17;
(c) bacteriophage fr;
(d) bacteriophage GA;
(e) bacteriophage SP;
(f) bacteriophage MS2;
(g) bacteriophage M11;
(h) bacteriophage MX1;
(i) bacteriophage NL95;
(j) bacteriophage f2;
(k) bacteriophage PP7; and
(l) bacteriophage AP205.

35. (currently amended) The composition of ~~any one of the preceding~~ claims 1, wherein said virus-like particle comprises~~, or alternatively consists essentially of, or alternatively consists of~~ recombinant proteins, or fragments thereof, of bacteriophage Qβ or bacteriophage AP205.

36. (currently amended) A method for enhancing an immune response against an antigen in an animal comprising introducing ~~into said animal a~~ the composition of ~~any one of the preceding~~ claims 1 into said animal, wherein an enhanced immune response against said antigen is produced in said animal.

37. (original) A method of producing a composition for enhancing an immune response in an animal comprising a virus-like particle and an immunostimulatory substance bound to said virus-like particle which comprises:

(a) incubating said virus-like particle with said immunostimulatory substance;

(b) adding RNase; and

(c) purifying said composition;

wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide, wherein the CpG motif of said unmethylated CpG-containing oligonucleotide is part of a palindromic sequence, and wherein said palindromic sequence is flanked at its 3'-terminus and at its 5'-terminus by less than 10 guanosine entities.

38. (cancelled)

39. (cancelled)

40. (cancelled)

41. (cancelled)

42. (cancelled)

43. (cancelled)

44. (cancelled)

45. (cancelled)

46. (cancelled)

47. (cancelled)

48. (cancelled)

49. (cancelled)

50. (currently amended) The method of ~~any of~~ claims 37 ~~to 49~~, further comprising the step of binding an antigen or antigenic determinant to said virus-like particle.

51. (cancelled)

52. (cancelled)

53. (original) A method of producing a composition for enhancing an immune response in an animal comprising a virus-like particle and an immunostimulatory substance bound to said virus-like particle which comprises:

(a) incubating said virus-like particle with RNase;

(b) adding said immunostimulatory substance; and

(c) purifying said composition

wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide, wherein the CpG motif of said unmethylated CpG-containing oligonucleotide is part of a palindromic sequence, and wherein said palindromic sequence is flanked at its 3'-terminus and at its 5'-terminus by less than 10 guanosine entities.

54. (cancelled)

55. (cancelled)

56. (cancelled)

57. (cancelled)

58. (cancelled)

59. (cancelled)

60. (cancelled)

61. (cancelled)

62. (cancelled)

63. (cancelled)

64. (cancelled)

65. (cancelled)

66. (currently amended) The method of ~~any of~~ claims 53 ~~to 65,~~ further comprising the step of binding an antigen or antigenic determinant to said virus-like particle.

67. (cancelled)

68. (cancelled)

69. (original) A method of producing a composition for enhancing an immune response in an animal comprising a virus-like particle and an immunostimulatory substance bound to said virus-like particle which comprises:

(a) disassembling said virus-like particle;

(b) adding said immunostimulatory substance; and

(c) reassembling said virus-like particle

wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide, wherein the CpG motif of said unmethylated CpG-containing oligonucleotide is part of a palindromic sequence, and wherein said palindromic sequence is flanked at its 3'-terminus and at its 5'-terminus by less than 10 guanosine entities.

70. (cancelled)

71. (cancelled)

72. (cancelled)

73. (cancelled)

74. (cancelled)

75. (cancelled)

76. (cancelled)

77. (cancelled)

78. (cancelled)

79. (cancelled)

80. (currently amended) The method of ~~any of~~ claims 69 ~~to 79~~ further comprising removing nucleic acids of said disassembled virus-like particle.

81. (cancelled)

82. (currently amended) The method of ~~any of~~ claims 69 ~~to 81,~~ further comprising the step of binding an antigen or antigenic determinant to said virus-like particle.

83. (cancelled)

84. (cancelled)

85. (original) A method of producing a composition for enhancing an immune response in an animal comprising a virus-like particle and an immunostimulatory substance bound to said virus-like particle which comprises:

(a) incubating said virus-like particle with solutions comprising metal ions capable of hydrolizing the nucleic acids of said virus-like particle;

(b) adding said immunostimulatory substance; and

(c) purifying said composition

wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide, wherein the CpG motif of said unmethylated CpG-containing oligonucleotide is part of a palindromic sequence, and wherein said palindromic sequence is flanked at its 3'-terminus and at its 5'-terminus by less than 10 guanosine entities.

86. (cancelled)

87. (cancelled)

88. (cancelled)

89. (cancelled)

90. (cancelled)

91. (cancelled)

92. (cancelled)

93. (cancelled)

94. (cancelled)

95. (cancelled)

96. (original) The method of claim 85, wherein said metal ions are selected from the group consisting of:

    (a) zinc (Zn) ions;

    (b) copper (Cu) ions;

    (c) iron (Fe) ions; and

    (d) any mixtures of at least one ion of (a), (b) and/or (c).

97. (currently amended) The method of ~~any of~~ claims 85 ~~to 96,~~ further comprising the step of binding an antigen or antigenic determinant to said virus-like particle.

98. (original) The method of claim 97, wherein said antigen or antigenic determinant is bound to said virus-like particle before incubating said virus-like particle with solutions comprising metal ions.

99. (original) The method of claim 50, wherein said antigen or antigenic determinant is bound to said virus like particle after adding said immunostimulatory substance and after purifying said composition.

100. (currently amended) A vaccine comprising an immunologically effective amount of the composition of ~~any one of~~ claim 1 ~~to 31~~ together with a pharmaceutically acceptable diluent, carrier or excipient.

101. (cancelled)

102. (currently amended) A method of immunizing or treating an animal comprising administering to said animal an immunologically effective amount of the vaccine of ~~any one of~~ claim 100 ~~or 101~~.

103. (cancelled)

104. (cancelled)

105. (cancelled)

106. (cancelled)

107. (currently amended) A method of immunizing or treating an animal comprising the steps of priming a T cell response in said animal, and boosting a T cell response in said animal, wherein said priming or said boosting is effected by administering an immunologically effective amount of the vaccine of claim 100.

108. (currently amended) The method of claim 107, wherein said ~~priming~~ priming and said boosting is effected by administering an immunologically effective amount of a vaccine of claim 100 ~~or an immunologically effective amount of a heterologous vaccine, and wherein even more preferably said heterologous vaccine is a DNA vaccine~~.

109. (currently amended) An isolated nucleic acid molecule ~~comprising, or alternatively consisting essentially of, or alternatively~~ consisting of an unmethylated CpG-containing oligonucleotide, wherein the CpG motif of said unmethylated CpG-containing oligonucleotide is part of a palindromic sequence, wherein said palindromic sequence is GACGATCGTC (SEQ ID NO: 1), and said palindromic sequence is flanked at its 5'-terminus of at least 4 and at most 9 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus of at least 6 and at most 9 guanosine entities.

110. (cancelled)

111. (cancelled)

112. (cancelled)

113. (cancelled)